

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

ANGEL et al.

)
) Applications
)

Serial No. Not Assigned

Filed:

For: SOFT CAPSULES COMPRISING POLYMERS OF VINYL ESTERS
AND POLYETHERS, THE USE AND PRODUCTION THEREOF

PRELIMINARY AMENDMENT

Hon. Commissioner of Patents and Trademarks
Washington, D.C. 20231

Sir:

Prior to examination, kindly amend the above-identified application as follows.

IN THE CLAIMS

Please amend the claims as shown in the attached sheets.


REMARKS

The claims have been amended to eliminate multiple dependency. No new matter has been added. A clean copy of the claims is attached.

Entry of the above amendment is respectfully solicited.

Respectfully submitted,

KEIL & WEINKAUF

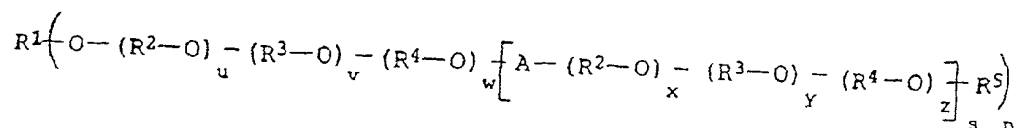

Herbert B. Keil
Reg. No. 18,967

1101 Connecticut Ave., N.W.
Washington, D.C. 20036
(202)659-0100

PRELIMINARY AMENDMENT -OZ 51248

3. A soft capsule as claimed in claim 1 [either of claims 1 or 2], wherein the polymers (a) are obtainable by free-radical polymerization of

- a) at least one vinyl ester of C₁-C₂₄-carboxylic acids in the presence of
- b) polyether-containing compounds of the general formula I



in which the variables have, independently of one another, the following meaning:

R¹ hydrogen, C₁-C₂₄-alkyl, R⁶-C(=O)-, R⁶-NH-C(=O)-, polyalcohol residue;

R⁵ hydrogen, C₁-C₂₄-alkyl, R⁶-C(=O)-, R⁶-NH-C(=O)-;

R² to R⁴

-(CH₂)₂-, -(CH₂)₃-, -(CH₂)₄-, -CH₂-CH(R⁶)-, CH₂-CHOR⁷-CH₂-;

R⁶ C₁-C₂₄-alkyl;

R⁷ hydrogen, C₁-C₂₄-alkyl, R⁶-C(=O)-, R⁶-NH-C(=O)-;

A -C(=O)-O-, -C(=O)-B-C(=O)-O-,

-C(=O)-NH-B-NH-C(=O)-O-;

B -(CH₂)_t-, arylene, optionally substituted;

n 1 to 1000;

s 0 to 1000;

t 1 to 12;

CLAIMS AMENDED IN PRELIMINARY AMENDMENT OZ 51248

u 1 to 5000;

v 0 to 5000;

w 0 to 5000;

x 0 to 5000;

y 0 to 5000;

z 0 to 5000;

and

c) where appropriate one or more other copolymerizable monomers

and subsequent at least partial hydrolysis of the ester functions in the original monomers a) .

4. A soft capsule as claimed in claim 1 [any of claims 1 to 3], wherein the polymers (a) are obtainable by free-radical polymerization of

a) at least one vinyl ester of C₁-C₂₄-carboxylic acids in the presence of

b) polyether-containing compounds of the general formula I with a number average molecular weight of from 300 to 100000, in which the variables have, independently of one another, the following meaning:

R¹ hydrogen, C₁-C₁₂-alkyl, R⁶-C(=O)- R⁶-NH-C(O), polyalcohol residue;

R⁵ hydrogen, C₁-C₁₂-alkyl, R⁶-C(=O)-, R⁶-NH-C(=O)-;

R² to R⁴

-(CH₂)₂-, -(CH₂)₃-, -(CH₂)₄-, -CH₂-CH(R⁶)-

-CH₂-CHOR⁷-CH₂-;

CLAIMS AMENDED IN PRELIMINARY AMENDMENT OZ 51248

R⁶ C₁-C₁₂-alkyl;

R⁷ hydrogen, C₁-C₁₂-alkyl, R⁶-C(=O)-, R⁶-NH-C(=O)-;

n 1 to 8;

s 0;

u 2 to 2000;

v 0 to 2000;

w 0 to 2000;

and

c) where appropriate one or more other copolymerizable monomers

and subsequent at least partial hydrolysis of the ester functions in the original

monomers a) .

5. A soft capsule as claimed in claim 1 [any of claims 1 to 4], wherein the polymers

(a) are obtainable by free-radical polymerization of

a) at least one vinyl ester of C₁-C₂₄-carboxylic acids in the presence of

b) polyether-containing compounds of the general formula I with a number average

molecular weight of from 500 to 50000, in which the variables have

independently of one another, the following meaning:

R¹ hydrogen, C₁-C₆-alkyl, R⁶-C(=O)-, R⁶-NH-C(=O)-;

R⁵ hydrogen, C₁-C₆-alkyl, R⁶-C(=O)-, R⁶-NH-C(=O)-;

R² to R⁴

-(CH₂)₂-, -(CH₂)₃-, -(CH₂)₄-, CH₂-CH(R⁶)-,

CLAIMS AMENDED IN PRELIMINARY AMENDMENT OZ 51248



R⁶ C₁-C₆-alkyl;

R⁷ hydrogen, C₁-C₆-alkyl, R⁶-C(=O)-, R⁶-NH-C(=O)-;

n 1;

s 0;

u 5 to 1000;

v 0 to 1000;

w 0 to 1000;

and

c) where appropriate one or more other copolymerizable monomers

and subsequent at least partial hydrolysis of the ester functions in the original monomers a).

6 A soft capsule as claimed in claim 1 [any of claims 1 to 5], wherein the polymers

(a) are obtainable by free-radical polymerization of

a) at least one vinyl ester of C₁-C₂₄-carboxylic acids in the presence of

b) polyether-containing compounds and

c) where appropriate one or more other copolymerizable monomers

and subsequent at least partial hydrolysis of the ester functions in the original

monomers a) , wherein the polyether-containing compounds b) have been prepared by

polymerization of ethylenically unsaturated alkylene oxide-containing monomers and,

where appropriate, other copolymerizable monomers.

CLAIMS AMENDED IN PRELIMINARY AMENDMENT OZ 51248

9. A soft capsule as claimed in claim 1 [any of claims 1 to 8], wherein the other copolymerizable monomer c) is selected from the group of:

acrylic acid, methacrylic acid, maleic acid, fumaric acid, crotonic acid, maleic anhydride and its monoesters, methyl acrylate, methyl methacrylate, ethyl acrylate, ethyl

methacrylate, n-butyl acrylate, n-butyl methacrylate, t-butyl acrylate, t-butyl

methacrylate, isobutyl acrylate, isobutyl methacrylate, 2-ethylhexyl acrylate, stearyl

acrylate, stearyl methacrylate, N-t-butylacrylamide, N-octylacrylamide, 2-hydroxyethyl

acrylate, hydroxypropyl acrylates, 2-hydroxyethyl methacrylate, hydroxypropyl

methacrylates, alkylene glycol (meth)acrylates, styrene, unsaturated sulfonic acids

such as, for example,

acrylamidopropanesulfonic acid, vinylpyrrolidone, vinylcaprolactam, vinyl ethers (for

example: methyl, ethyl, butyl or dodecyl vinyl ether) , vinylformamide,

vinylmethylacetamide, vinylamine, 1-vinylimidazole, 1-vinyl-1-methyylimidazole, N,N-

dimethylaminomethyl methacrylate and N-[3-(dimethylamino)propyl]methacrylamide; 3-

methyl-1-vinylimidazolium chloride, 3-methyl-1-vinylimidazolium methyl sulfate, N,N-

dimethylaminoethyl methacrylate, N-[3-(dimethylamino)- propyl]methacrylamide

quaternized with methyl chloride methyl sulfate or diethyl sulfate.

10. A soft capsule as claimed in claim 1 [any of claims 1 to 9], wherein the ratios of amounts are

a) 10 to 98% by weight

b) 2 to 90% by weight

CLAIMS AMENDED IN PRELIMINARY AMENDMENT OZ 51248

c) 0 to 50% by weight.

11. A soft capsule as claimed in claim 1 [any of claims 1 to 10], wherein the ratios of amounts are

a) 50 to 97% by weight

b) 3 to 50% by weight

c) 0 to 20% by weight.

12. A soft capsule as claimed in claim 1 [any of claims 1 to 11], wherein the ratios of amounts are

a) 65 to 97% by weight

b) 3 to 35% by weight

c) 0 to 20% by weight .

13. A soft capsule as claimed in claim 1 [any of claims 1 to 12], wherein the resulting polymers are subsequently crosslinked by a polymer-analogous reaction.

14. A soft capsule as claimed in claim 1 [any of claims 1 to 13], wherein aldehydes, diketones, dicarboxylic acids, boric acid, boric acid salts, and salts of multiply charged cations are employed for the subsequent crosslinking.

15. A soft capsule as claimed in claim 1 [any of claims 1 to 14], wherein the structure-improving auxiliaries (b) employed are compounds from the following classes:

a) [Polymers] polymers with a molecular weight of more than 50000

b) substances leading to crosslinking of the polymer chains of the polymers,

c) and, where appropriate, substances which lead to crosslinking of the

CLAIMS AMENDED IN PRELIMINARY AMENDMENT OZ 51248

polymer chains of the structure-improving auxiliaries.

16. A soft capsule as claimed in claim 1 [any of claims 1 to 15], wherein the structure-improving auxiliaries employed are polymers from the following classes of substances:

polyamino acids such as gelatin, zein, soybean protein and derivatives thereof, polysaccharides such as starch, degraded starch, maltodextrins, carboxymethylstarch, cellulose, hydroxypropylmethylcellulose, hydroxypropylcellulose, hydroxyethylcellulose, methylcellulose, carboxymethylcellulose, ethylcellulose, cellulose acetate, cellulose acetate phthalate, hydroxypropylcellulose acetate phthalate, hydroxypropylcellulose acetate succinate, hemicellulose, galactomannans, pectins, alginates, carrageenans, xanthan, gellan, dextran, curdlan, pullulan, gum arabic, chitin, and derivatives thereof, synthetic polymers such as polyacrylic acid, polymethacrylic acid, copolymers of acrylic esters and methacrylic esters, polyvinyl alcohols, polyvinyl acetate, polyethylene glycols, polyoxyethylene/polyoxypropylene block copolymers, polyvinylpyrrolidones and derivatives thereof.

17. A soft capsule as claimed in claim 1 [any of claims 1 to 16], wherein other conventional constituents of the shell which are present are fillers, release agents, flow aids, dyes, pigments, opacifiers, flavorings, sweeteners, plasticizers, preservatives and/or active ingredients.

18. A soft capsule as claimed in claim 1 [any of claims 1 to 17], wherein the shell consists of from 10 to 100% by weight of polymers of vinyl esters on polyether, where

CLAIMS AMENDED IN PRELIMINARY AMENDMENT OZ 51248

appropriate from 0 to 80% of structure-improving auxiliaries and, where appropriate, from 0 to 30% of other conventional constituents.

19. A soft capsule as claimed in claim 1 [any of claims 1 to 18], obtainable by processes such as the rotary die process, Accogel process, Norton process, drop or blow process or the Colton-Upjohn process.

20. A soft capsule as claimed in claim 1 [any of claims 1 to 19], which comprises one or more active pharmaceutical ingredients, vitamins, carotenoids, minerals, trace elements, food supplements, cosmetic active ingredients, crop protection agents, bath additives, perfume, flavoring, cleaner or detergent.

21. A soft capsule as claimed in claim 1 [any of claims 1 to 20], wherein the shell comprises from 20 to 80% of a polymer resistant to gastric fluid.

22. A soft capsule as claimed in claim 1 [any of claims 1 to 21], wherein resistance to gastric fluid is achieved by applying after production a coating resistant to gastric fluid by conventional pharmaceutical coating processes.

23. The use of the soft capsules as claimed in claim 1 [any of claims 1 to 22] for pharmaceutical applications.

24. The use of the soft capsules claimed in claim 1 [any of claims 1 to 22] for cosmetic applications, applications in crop protection, for cleaners or food supplements.

25. The use of polymers obtainable by free-radical polymerization of

- a) at least one vinyl ester of C_1 - C_{24} -carboxylic acids in the presence of

CLAIMS AMENDED IN PRELIMINARY AMENDMENT OZ 51248

b) polyether-containing compounds and

c) where appropriate one or more copolymerizable monomers

and subsequent at least partial hydrolysis of the ester functions in the original

monomers a) to produce soft capsules as claimed in claim 1 [any of claims 1 to 22].

26. The use of polymers obtainable by free-radical polymerization of

a) at least one vinyl ester of C₁-C₂₄-carboxylic acids in the presence of

b) polyether-containing compounds and

c) where appropriate one or more copolymerizable monomers

and subsequent at least partial hydrolysis of the ester functions in the original

monomers a) wherein the polyether-containing compounds b) have been prepared by

polymerization of ethylenically unsaturated alkylene oxide-containing monomers and,

where appropriate, other copolymerizable monomers, for producing soft capsules as

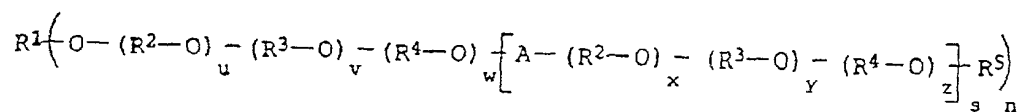
claimed in claim 1 [any of claims 1 to 22].

CLAIMS AS FILED IN PRELIMINARY AMENDMENT -OZ 51248

1. A soft capsule comprising
 - (a) polymers prepared by polymerization of vinyl esters in the presence of polyethers
 - (b) where appropriate structure-improving auxiliaries and
 - (c) where appropriate other conventional constituents .
2. A soft capsule as claimed in claim 1, wherein the polymers
 - (a) are obtainable by free-radical polymerization of
 - a) at least one vinyl ester of C₁-C₂₄-carboxylic acids in the presence of
 - b) polyether-containing compounds and
 - c) where appropriate one or more copolymerizable monomers

and subsequent at least partial hydrolysis of the ester functions in the original monomers a) .

3. A soft capsule as claimed in claim 1, wherein the polymers (a) are obtainable by free-radical polymerization of
 - a) at least one vinyl ester of C₁-C₂₄-carboxylic acids in the presence of
 - b) polyether-containing compounds of the general formula I



in which the variables have, independently of one another, the following meaning:

R¹ hydrogen, C₁-C₂₄-alkyl, R⁶-C(=O)-, R⁶-NH-C(=O)-, polyalcohol residue;

R⁵ hydrogen, C₁-C₂₄-alkyl, R⁶-C(=O)-, R⁶-NH-C(=O)-;

R² to R⁴

-(CH₂)₂-, -(CH₂)₃-, -(CH₂)₄-, -CH₂-CH(R⁶)-, CH₂-CHOR⁷-CH₂-;

R⁶ C₁-C₂₄-alkyl;

R⁷ hydrogen, C₁-C₂₄-alkyl, R⁶-C(=O)-, R⁶-NH-C(=O)-;

A -C(=O)-O-, -C(=O)-B-C(=O)-O-,

-C(=O)-NH-B-NH-C(=O)-O-;

B -(CH₂)_t-, arylene, optionally substituted;

n 1 to 1000;

s 0 to 1000;

t 1 to 12;

u 1 to 5000;

v 0 to 5000;

w 0 to 5000;

x 0 to 5000;

y 0 to 5000;

z 0 to 5000;

and

c) where appropriate one or more other copolymerizable monomers

and subsequent at least partial hydrolysis of the ester functions in the original monomers a) .

4. A soft capsule as claimed in claim 1, wherein the polymers (a) are obtainable by free-radical polymerization of

- a) at least one vinyl ester of C_1 - C_{24} -carboxylic acids in the presence of
- b) polyether-containing compounds of the general formula I with a number average molecular weight of from 300 to 100000, in which the variables have, independently of one another, the following meaning:

R^1 hydrogen, C_1 - C_{12} -alkyl, R^6 -C(=O)-, R^6 -NH-C(=O), polyalcohol residue;

R^5 hydrogen, C_1 - C_{12} -alkyl, R^6 -C(=O)-, R^6 -NH-C(=O)-;

R^2 to R^4

$-(CH_2)_2-$, $-(CH_2)_3-$, $-(CH_2)_4-$, $-CH_2-CH(R^6)-$

$-CH^2-CHOR^7-CH_2-$;

R^6 C_1 - C_{12} -alkyl;

R^7 hydrogen, C_1 - C_{12} -alkyl, R^6 -C(=O)-, R^6 -NH-C(=O)-;

n 1 to 8;

s 0;

u 2 to 2000;

v 0 to 2000;

w 0 to 2000;

and

- c) where appropriate one or more other copolymerizable monomers

and subsequent at least partial hydrolysis of the ester functions in the original monomers a) .

5. A soft capsule as claimed in claim 1, wherein the polymers (a) are obtainable by free-radical polymerization of

- a) at least one vinyl ester of C₁-C₂₄-carboxylic acids in the presence of
- b) polyether-containing compounds of the general formula I with a number average molecular weight of from 500 to 50000, in which the variables have independently of one another, the following meaning:

R¹ hydrogen, C₁-C₆-alkyl, R⁶-C(=O)-, R⁶-NH-C(=O)-;

R⁵ hydrogen, C₁-C₆-alkyl, R⁶-C(=O)-, R⁶-NH-C(=O)-;

R² to R⁴

-(CH₂)₂-, -(CH₂)₃-, -CH₂)₄-, CH₂-CH(R⁶)-,

-CH²-CHOR⁷-CH₂-;

R⁶ C₁-C₆-alkyl;

R⁷ hydrogen, C₁-C₆-alkyl, R⁶-C(=O)-, R⁶-NH-C(=O)-;

n 1;

s 0;

u 5 to 1000;

v 0 to 1000;

w 0 to 1000;

and

- c) where appropriate one or more other copolymerizable monomers

and subsequent at least partial hydrolysis of the ester functions in the original monomers a).

6. A soft capsule as claimed in claim 1, wherein the polymers (a) are obtainable by free-radical polymerization of

- a) at least one vinyl ester of C_1 - C_{24} -carboxylic acids in the presence of
- b) polyether-containing compounds and
- c) where appropriate one or more other copolymerizable monomers

and subsequent at least partial hydrolysis of the ester functions in the original monomers a) , wherein the polyether-containing compounds b) have been prepared by polymerization of ethylenically unsaturated alkylene oxide-containing monomers and, where appropriate, other copolymerizable monomers.

7. A soft capsule as claimed in claim 6, wherein the polyether-containing compounds b) have been prepared by polymerization of polyalkylene oxide vinyl ethers and, where appropriate, other copolymerizable monomers.

8. A soft capsule as claimed in claim 6, wherein the polyether-containing compounds b) have been prepared by polymerization of polyalkylene oxide (meth)acrylates and where appropriate, other copolymerizable monomers.

9. A soft capsule as claimed in claim 1, wherein the other copolymerizable monomer c) is selected from the group of:

acrylic acid, methacrylic acid, maleic acid, fumaric acid, crotonic acid, maleic anhydride and its monoesters, methyl acrylate, methyl methacrylate, ethyl acrylate, ethyl methacrylate, n-butyl acrylate, n-butyl methacrylate, t-butyl acrylate, t-butyl methacrylate, isobutyl acrylate, isobutyl methacrylate, 2-ethylhexyl acrylate, stearyl acrylate, stearyl methacrylate, N-t-butylacrylamide, N-octylacrylamide, 2-hydroxyethyl

acrylate, hydroxypropyl acrylates, 2-hydroxyethyl methacrylate, hydroxypropyl methacrylates, alkylene glycol (meth)acrylates, styrene, unsaturated sulfonic acids such as, for example, acrylamidopropanesulfonic acid, vinylpyrrolidone, vinylcaprolactam, vinyl ethers (for example: methyl, ethyl, butyl or dodecyl vinyl ether) , vinylformamide, vinylmethylacetamide, vinylamine, 1-vinylimidazole, 1-vinyl-1-methylimidazole, N,N-dimethylaminomethyl methacrylate and N-[3-(dimethylamino)propyl]methacrylamide; 3-methyl-1-vinylimidazolium chloride, 3-methyl-1-vinylimidazolium methyl sulfate, N,N-dimethylaminoethyl methacrylate, N-[3-(dimethylamino)- propyl]methacrylamide quaternized with methyl chloride methyl sulfate or diethyl sulfate.

10. A soft capsule as claimed in claim 1, wherein the ratios of amounts are

- a) 10 to 98% by weight
- b) 2 to 90% by weight
- c) 0 to 50% by weight.

11. A soft capsule as claimed in claim 1, wherein the ratios of amounts are

- a) 50 to 97% by weight
- b) 3 to 50% by weight
- c) 0 to 20% by weight.

12. A soft capsule as claimed in claim 1, wherein the ratios of amounts are

- a) 65 to 97% by weight
- b) 3 to 35% by weight
- c) 0 to 20% by weight .

13. A soft capsule as claimed in claim 1, wherein the resulting polymers are subsequently crosslinked by a polymer-analogous reaction.

14. A soft capsule as claimed in claim 1, wherein dialdehydes, diketones, dicarboxylic acids, boric acid, boric acid salts, and salts of multiply charged cations are employed for the subsequent crosslinking.

15. A soft capsule as claimed in claim 1, wherein the structure-improving auxiliaries (b) employed are compounds from the following classes:

- a) polymers with a molecular weight of more than 50000
- b) substances leading to crosslinking of the polymer chains of the polymers,
- c) and, where appropriate, substances which lead to crosslinking of the polymer chains of the structure-improving auxiliaries.

16. A soft capsule as claimed in claim 1, wherein the structure-improving auxiliaries employed are polymers from the following classes of substances:

polyamino acids such as gelatin, zein, soybean protein and derivatives thereof, polysaccharides such as starch, degraded starch, maltodextrins, carboxymethylstarch, cellulose, hydroxypropylmethylcellulose, hydroxypropylcellulose, hydroxyethylcellulose, methylcellulose, carboxymethylcellulose, ethylcellulose, cellulose acetate, cellulose acetate phthalate, hydroxypropylcellulose acetate phthalate, hydroxypropylcellulose acetate succinate, hemicellulose, galactomannans, pectins, alginates, carrageenans, xanthan, gellan, dextran, curdlan, pullulan, gum arabic, chitin, and derivatives thereof, synthetic polymers such as polyacrylic acid, polymethacrylic acid, copolymers of acrylic esters and methacrylic esters, polyvinyl alcohols, polyvinyl acetate, polyethylene

glycols, polyoxyethylene/polyoxypropylene block copolymers, polyvinylpyrrolidones and derivatives thereof.

17. A soft capsule as claimed in claim 1, wherein other conventional constituents of the shell which are present are fillers, release agents, flow aids, dyes, pigments, opacifiers, flavorings, sweeteners, plasticizers, preservatives and/or active ingredients.

18. A soft capsule as claimed in claim 1, wherein the shell consists of from 10 to 100% by weight of polymers of vinyl esters on polyether, where appropriate from 0 to 80% of structure-improving auxiliaries and, where appropriate, from 0 to 30% of other conventional constituents.

19. A soft capsule as claimed in claim 1, obtainable by processes such as the rotary die process, Accogel process, Norton process, drop or blow process or the Colton-Upjohn process.

20. A soft capsule as claimed in claim 1, which comprises one or more active pharmaceutical ingredients, vitamins, carotenoids, minerals, trace elements, food supplements, cosmetic active ingredients, crop protection agents, bath additives, perfume, flavoring, cleaner or detergent.

21. A soft capsule as claimed in claim 1, wherein the shell comprises from 20 to 80% of a polymer resistant to gastric fluid.

22. A soft capsule as claimed in claim 1, wherein resistance to gastric fluid is achieved by applying after production a coating resistant to gastric fluid by conventional pharmaceutical coating processes.

23. The use of the soft capsules as claimed in claim 1 for pharmaceutical

applications.

24. The use of the soft capsules claimed in claim 1 for cosmetic applications, applications in crop protection, for cleaners or food supplements.

25. The use of polymers obtainable by free-radical polymerization of

- a) at least one vinyl ester of C_1 - C_{24} -carboxylic acids in the presence of
- b) polyether-containing compounds and
- c) where appropriate one or more copolymerizable monomers

and subsequent at least partial hydrolysis of the ester functions in the original monomers a) to produce soft capsules as claimed in claim 1.

26. The use of polymers obtainable by free-radical polymerization of

- a) at least one vinyl ester of C_1 - C_{24} -carboxylic acids in the presence of
- b) polyether-containing compounds and
- c) where appropriate one or more copolymerizable monomers

and subsequent at least partial hydrolysis of the ester functions in the original

monomers a) wherein the polyether-containing compounds b) have been prepared by polymerization of ethylenically unsaturated alkylene oxide-containing monomers and, where appropriate, other copolymerizable monomers, for producing soft capsules as claimed in claim 1.